

# nih record



**ABOVE** • Bare against the July sky is NIH's Tree of Hippocrates, which is ailing. See story on p. 12.

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*The CC's 'Tree of Life'*

### Patient's Mother Brings Art, Joy to Pediatric Rooms

By Belle Waring

**T**here are trees painted on the windows in the Clinical Center—trees with welcoming branches like the arms of an old friend.

These are the creation of special volunteer Annette Weller, a self-taught artist who decorates the pediatric unit with her original work.

Weller is the mother of Lauren Marie Weller Sidorowicz, who received treatment at NIH for Ewing's sarcoma, a type of cancer. Diagnosed at age 18, Lauren spent 8 years on many different NIH protocols, both pediatric and adult. She passed away on Dec. 14, 2011.

"Lauren had many inpatient stays with surgeries, chemo and radiation," said Weller. "She was one of the first of the Ewing's transplants; her sister Lindsay donated stem cells. So this was a home for us. They took us in and wrapped their arms around us. Doctors, nurses, guys parking the cars, the front desk, the people who make the coffee..."

SEE WINDOW ART, PAGE 6



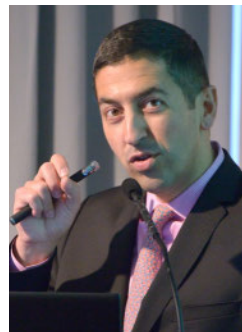
Lauren Sidorowicz enjoys a U2 concert in Baltimore in summer 2011.

*'Move the Whole Curve'*

### Galea Calls for Re-engagement in Population Health

By Belle Waring

In Greek mythology, Prometheus, champion of humanity, stole fire from heaven and delivered it to mortals on Earth. Zeus, king of the gods, was so enraged by the theft that he sentenced Prometheus to be chained to a rock in eternal torment.



Dr. Sandro Galea

That Promethean fire of human progress foretells modern science. Yet unlike Prometheus, we who work in biomedical research and public health are *expected* to challenge prevailing wisdom. To question assumptions is crucial to the scientific method, which is designed to let reality speak for itself.

SEE GALEA, PAGE 8

### CC Celebrates 60 Years of Medical Discovery with Special Grand Rounds

By Nicole Martino

The Clinical Center's first patient—Charles Meredith, a Maryland farmer with prostate cancer—was admitted to the brand new facility on July 6, 1953. Sixty years and nearly a half a million patients later, NIH celebrated the hospital's role in discovering tomorrow's cures with a special Grand Rounds/Contemporary Clinical Medicine: Great Teachers presentation in Masur Auditorium on July 10.

The Grand Rounds featured lectures by Dr. James F. Holland, a cancer researcher who worked at the CC at its opening 60 years ago, and his son, Dr. Steven M. Holland, chief of the NIAID Laboratory of Clinical Infectious Diseases and NIH deputy director for intramural clinical research.

The senior Holland, distinguished professor of neoplastic diseases at Icahn School of Medicine at Mount Sinai, is a pioneer in clinical cancer research. He contributed to the first com-

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**NIH Record Office** Bldg. 31, Rm. 5B41  
**Phone** (301) 496-2125 **Fax** (301) 402-1485

**Web address** <http://nihrecord.od.nih.gov>

**Editor**  
Richard McManus  
[Rich.McManus@nih.gov](mailto:Rich.McManus@nih.gov)

**Associate Editor**  
Carla Garnett  
[Carla.Garnett@nih.gov](mailto:Carla.Garnett@nih.gov)

**Staff Writers**  
Jan Ehrman  
[Jan.Ehrman@nih.gov](mailto:Jan.Ehrman@nih.gov)

Dana Steinberg  
[Dana.Steinberg@nih.gov](mailto:Dana.Steinberg@nih.gov)

Belle Waring  
[Belle.Waring@nih.gov](mailto:Belle.Waring@nih.gov)

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*NIH...Turning Discovery Into Health*

## briefs

### Free Outdoor Film Festival Goes 'Drive In'

The 17th annual Comcast Outdoor Film Festival will take place Friday, Aug. 16 - Sunday, Aug. 18 at the MCPS Board of Education Bldg. at 850 Hungerford Dr., Rockville. The location was once the site of a drive-in movie theater so the event pays homage to an old tradition. This year's festival will be a drive-in, so watch the movies on a 52-foot-wide screen from the comfort of your car. You can also watch the movies on the lawn—just bring your blanket, chairs (low chairs only) and anyone who loves movies. Festivities begin at 5:30 p.m. and the movies begin at dusk. They include:

*Oz: The Great and Powerful* (Aug. 16)

*Skyfall* (Aug. 17)

*The Amazing Spider-Man* (Aug. 18)

The movies are free and food and drinks will be available to purchase. There will also be a raffle and donations will be accepted to help raise funds for the NIH Charities (Friends of the Clinical Center, Children's Inn and Camp Fantastic/Special Love). Contact Kallie Wasserman at [wassermankt@mail.nih.gov](mailto:wassermankt@mail.nih.gov) if you're interested in volunteering. For more information, visit [www.filmfestnih.org](http://www.filmfestnih.org) or call (301) 816-6958.

### Summer Poster Day at Natcher, Aug. 8

Summer Poster Day 2013 is scheduled for Thursday, Aug. 8 at the Natcher Conference Center from 9 a.m. to 3 p.m. Summer interns will share research they have been conducting at NIH and develop their communication and networking skills. Any summer intern (high school, college, medical/dental or graduate) working in an intramural research group at NIH this summer may present. Investigators, staff scientists and scientific administrators can make an important contribution by visiting posters and discussing research with presenters. For details, visit [https://www.training.nih.gov/summer\\_poster\\_day](https://www.training.nih.gov/summer_poster_day).

### Photo Contest Focuses on Safety

Whether photography is your passion, hobby or just an occasional pastime, you are invited to participate in the Office of Research Services' 3rd annual "In Focus! Safe Workplaces for All" photo contest. Entries should display safe workplaces or activities, e.g., laboratory workers using personal protective equipment, crossing guards on busy streets, construction workers using safety gear, etc.

The goals are to help reduce injuries and illnesses; educate and underscore the importance of safety; foster innovation to create shared solutions; and promote community involvement by displaying NIH talent, imagination and creativity to raise awareness of workplace safety and health.

First, second and third place photographs will be framed and displayed outside the ORS office. The images will also appear on posters and publications throughout NIH and be featured on the Division of Occupational Health and Safety web site. The three winners will receive recognition and a framed certificate from NIH leadership.

The submission period began Aug. 1 and is open until Sept. 30. To learn more about the contest, rules, panel of judges, selection process and to submit your photo, visit [www.ors.od.nih.gov/sr/dohs/HealthAndSafety/infocus](http://www.ors.od.nih.gov/sr/dohs/HealthAndSafety/infocus).

### Claims of Transgender Discrimination Can Now Be Pursued with EEOC

Did you know that a claim of sex discrimination based on an individual's transgender status can now be pursued with the Equal Employment Opportunity Commission (EEOC)? On Apr. 20, in a landmark case (*Macy v. Department of Justice*), the EEOC held that discrimination against an individual because that person is transgender is a form of sex discrimination under Title VII.

Within the EEO complaint process, agencies can no longer dismiss cases raising transgender, gender identity, changes of sex and/or sex/gender stereotyping as a basis outside of Title VII. Employees can now file EEO complaints for this form of discrimination by electing "sex" as the basis of the complaint.

In light of the new developments, the Office of Equal Opportunity and Diversity Management has taken action to ensure compliance. OEODM provided an internal briefing for all staff members and had lengthy consultation with the Department of Health and Human Services to obtain its policy guidance based on the Macy decision. In consultation with Salutaris, and in conformance with HHS guidance, OEODM has updated informal and formal forms to align with recent developments. In addition, many of NIH's EEO counselors and formal complaints specialists attended briefings at the EEOC and HHS to fully understand the implications of Macy.

Equal employment opportunity laws are constantly changing and OEODM is committed to keeping abreast of the new developments and ensuring that the NIH community is informed. If you have any questions or would like more information, call (301) 496-6301.

# nih record



*Affects 36 Million People Worldwide*

## NINDS Sponsors Workshop on Alzheimer's Disease-Related Dementias

By Shannon E. Garnett

Alzheimer's disease accounts for most cases of dementia, however, about a third of all cases are caused by other, lesser known brain diseases. In fact, most people diagnosed with Alzheimer's do not have a pure form of the disease—instead they have a mix of Alzheimer's and other disorders. When all types of dementia are added together, as many as 36 million people in the world are living with the disorder; its burden is growing as our population ages.

How best to pursue scientific solutions to this daunting public health problem? NINDS recently sponsored a 2-day workshop, “Alzheimer's Disease-Related Dementias: Research Challenges and Opportunities,” to gather ideas.

Held at Natcher Conference Center, the meeting brought together scientists focused on dementia research as well as other experts from academia, industry and non-profit groups and patient caregivers to help guide scientific research and set priorities on Alzheimer's disease-related dementias (ADRD) for the next 5 to 10 years. ADRD—specifically defined for the conference as frontotemporal, Lewy body, mixed and vascular dementias—are debilitating conditions that impair memory, thought processes and functioning and occur primarily in older adults.

“We need to know what research paths will lead to major scientific advances for people who are facing dementia,” said NINDS deputy director Dr. Walter Koroshetz in welcoming remarks. “Are there fruitful research directions that we have not yet thought about? Without a conference like this, those new pursuits do not happen except by serendipity. We would like to attack the burden of illness due to dementia with a well-considered plan, not relying solely on serendipity.”

Dr. Ronald Petersen of the Mayo Clinic, chair of the Advisory Council on Alzheimer's Research, Care and Services, gave an overview of the National Alzheimer's Project Act (NAPA). The 2011 NAPA law led to the National Plan to Address Alzheimer's Disease. As part of that plan, NIA last year held the “Alzheimer's Disease Research Summit,” which created a multidisciplinary research agenda to accelerate development of AD therapies.

The national plan also called for NIH to hold a conference in 2013 to develop research priorities that will pave the way for treatments for dementias related to AD. NINDS's ADRD work-



*Approximately 500 people attended the ADRD workshop, which included presentations, panel discussions and (at left) opportunities for public comments. At right, NINDS deputy director Dr. Walter Koroshetz welcomes attendees.*

PHOTOS: BILL BRANSON

shop—organized in collaboration with NIA, the Alliance for Aging Research, the Alzheimer's Association, the Association for Frontotemporal Degeneration and USAgainst Alzheimer's—answered that call.

For months leading up to the meeting, groups of top dementia researchers, physicians and other experts worked to develop core recommendations. The ADRD workshop's purpose was to review, tweak and, perhaps most importantly, prioritize the recommendations.

“If everything is a top priority, then nothing is a top priority,” said Dr. Thomas Montine of the University of Washington, who served as scientific chair of the workshop. “We need to stay focused on a short list of highest priorities to be sure that we remain actionable.”

About 500 people attended the meeting, which featured 65 speakers and was divided into 5 sessions on major research areas: ADRD and Multiple Etiology Dementias, Lewy Body Dementias, Frontotemporal Dementia and AD-Related Tauopathies, Vascular Contributions to ADRD and Health Disparities in ADRD. At the end, chairs from each session fielded questions and collected feedback on the recommendations.

Several key ideas were shared:

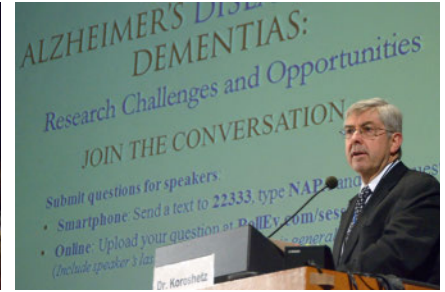
- ❑ Increase knowledge of disease mechanisms with a special emphasis on improving disease models to learn more about the fundamental biology of ADRD
- ❑ Aid preclinical development of new treatments
- ❑ Improve diagnostics for all types of dementia

Another theme was education—to help primary care physicians identify ADRD earlier, and more effectively treat Alzheimer's and ADRD, as well as increase awareness of the disorders among the public.

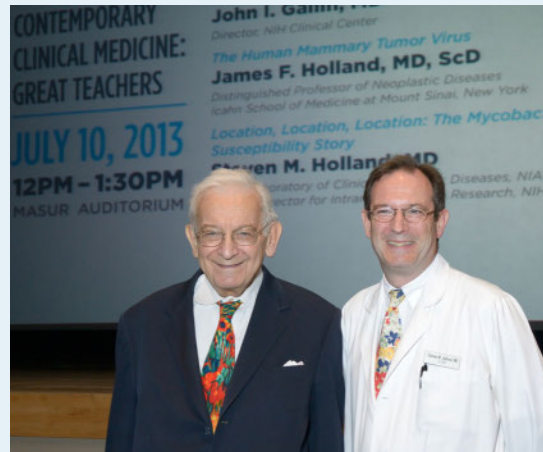
The meeting also highlighted the recent momentum boost to dementia research via NIH director Dr. Francis Collins' commitment of an additional \$40 million toward NIH Alzheimer's research in 2013, as well as the boost to neuroscience research in general through the new BRAIN Initiative.

Recommendations from the workshop will be presented to NINDS's advisory council in September and then to the NAPA council in October.

“I cannot overemphasize how important these discussions are to NIH,” concluded Koroshetz. “Our success in decreasing the burden of illness due to ADRDs is highly dependent upon this thoughtful scientific and stakeholder input.”



*Workshop scientific chair Dr. Thomas Montine (l) with workshop lead Dr. Roderick Corriveau*



## ANNIVERSARY

CONTINUED FROM PAGE 1

**Above from 1:** NIH deputy director for intramural research Dr. Michael Gottesman (l) chats with Dr. James F. Holland, who was on staff at the Clinical Center when the hospital opened in 1953.

CC director Dr. John Gallin presented a review of the hospital's 60 years of clinical research.

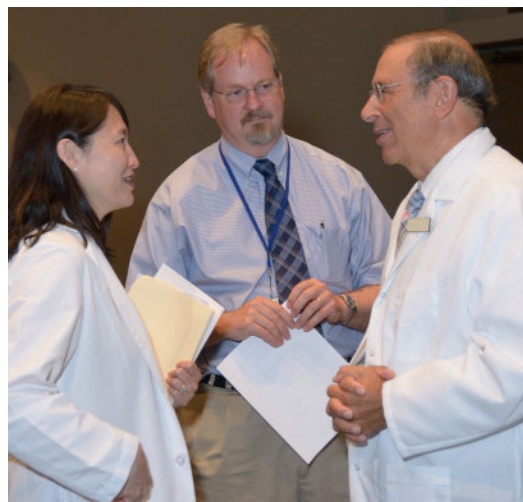
The father-son duo of Dr. James F. and Dr. Steven M. Holland hints at the family-centered nature of CC care.

PHOTOS: BILL BRANSON

combination chemotherapy in acute leukemia and helped transform what was once an incurable disease to a disease with an over 80 percent survival rate.

"I became interested in the proposition of what causes cancer," he said. "Most cancers arise from specific causes. The problem is we just don't know what those specific causes are most of the time." He presented on his research on the human mammary tumor virus, a virus that is present in 40 percent of American women's breast cancers that is 90-95 percent homologous to the mouse mammary tumor virus, a milk-transmitted virus that causes breast cancer in mice.

Steven followed his father. His presentation, "Location, Location, Location: The Mycobacterial Susceptibility Story," detailed his research on nontuberculous mycobacterial infections. "It turns out that where your problem is has a lot to do with what your problem is, and the first question to ask is not *what* is the organism involved but *where* is the organism involved," he said, emphasizing the focus on patient experience.



NIMH clinical director Dr. Maryland Pao (l) and NIDCD clinical director Dr. Carter VanWaes chat with Gallin at Grand Rounds.

"It starts with patients, it's complicated and confusing and it has lots of twists and turns but it's the most exciting thing out there and that is what the Clinical Center is all about," said Steven. "Here you have the guy who was here on day one talking about patient-centered research, and here we are today talking about the same thing. That is what 60 years of this place seems to be about."

CC director Dr. John Gallin also presented a review of the hospital's 60 years of clinical research, highlighting some of the advances and medical milestones accomplished throughout the center's history as well as in recent years. From the first HIV/AIDS treatments and digital medical record systems, to the discovery of the gene for stuttering and the discovery of autoimmune-inflammatory diseases, the accomplishments are too many to display, he said.

"All this started here," said Gallin. "So much of the standard of care in the United States, which we take for granted, originated in this building."

The lecture was a true reunion, complete with public display of embarrassing family photos and disclosures of guilty pleasures. The crowd in the auditorium, which swelled to more than 800 people including an overflow audience in Lipsett Amphitheater, and the reception that followed demonstrated the significance of the milestone to the CC community.

Gallin acknowledged that the CC and NIH mean different things to different people. "To some it's the buildings or grounds, to many it's the science, to the patients it's the care," he said. "But I think to everyone, it's the amazing group of people who work here that we get to interact with every day and who have been here before us."

For more information about the anniversary, including historical milestones and details about the celebration visit [www.clinicalcenter.nih.gov/about/news/annivers60.shtml](http://www.clinicalcenter.nih.gov/about/news/annivers60.shtml). 📺



## Parental Messages Take Hold on College Campuses, Research Indicates

By Jan Ehrman

College students—enjoy your summer break. You’ve earned it. But when you get back on campus, be sure to keep in touch with your folks. It’s good for your health, according to an NIH-funded study.

Despite the independence many college freshmen yearn for, data indicate that most first-year students expect their parents to provide counsel and assistance during and shortly after the transitional years.

How much influence parents have over their children’s activities during the first year of advanced learning remains ripe for investigation, as such a cause-and-effect link may predict future adult behaviors, experts suspect.



Dr. Meg Small


Dr. Meg Small, assistant director of the Prevention Research Center at Pennsylvania State University, and her associates investigated the protective effect of parent-student communication as it pertained to collegians’ eating and physical activity patterns. A total of 746 first-year college students participating in the long-running University Life Study filled out baseline surveys followed by 14 consecutive daily surveys during both semesters of their freshman year. Via the questionnaires, researchers monitored many of the students’ daily activities, with a focus on nutritional and exercise behaviors on days they communicated with their folks, as measured against days when there were no interactions.

“What we learned was that on days that the students communicated more with their parents (either by phone, text or email), they were significantly more likely to eat fruits and vegetables and spend more time exercising,” said Small, who acknowledged she was not sure there were direct messages or indirect ones coming from parents. In addition, although researchers did not look at what was discussed between parent and student, the amount of time each interaction took or how close a relation the parties had with each other (e.g., the “parental warmth” factor), the evidence revealed “a protective effect” from parents. It

also mimicked earlier investigations by Small involving alcohol consumption and parent-student communication. These findings showed that on days that freshman collegians communicated with their folks, they consumed fewer drinks, had a lower blood alcohol content and were less likely to binge, she explained.

The findings are noteworthy for both generations. “One of the real take-home messages and what stands out,” says Small, “is that parents still count. They really do. Based on our most recent findings, we see that they continue to have a significant influence on college behaviors at least in the first year of advanced schooling. And these behaviors could have an impact in later life.”

Meanwhile, other studies have shown that healthy behaviors such as proper nutrition and regular exercise typically decline in post-freshman years. Upcoming investigations by Small and her team will delve into whether there are subgroups in which declines in nutrition and exercise do not occur in college years 2-4 and what influence continued, regular communication between parent and child would have on those lifestyle factors.

Results of this study appeared in a recent issue of the *Journal of Adolescent Health* and were supported by the National Institute on Alcohol Abuse and Alcoholism. 

## NIAMS Advocates Tour Campus

NIAMS recently hosted a campus visit and laboratory tours for members of the NIAMS Coalition steering committee. The committee leads the activities of the coalition, a group of more than 80 volunteer and professional organizations devoted to promoting a better understanding of diseases of the bones, joints, muscles and skin.



NIAMS Coalition steering committee members and NIAMS senior leadership gather outside of Bldg. 50 during their campus visit.

The group heard from NIAMS senior leadership, including acting director Dr. Robert Carter, intramural clinical director Dr. Richard Siegel, extramural division directors Dr. Joan McGowan and Dr. Laura Moen, and Anita Linde, director of the Office of Science Policy, Planning and Communications.

The committee also visited three NIAMS labs: Dr. Mahendra Rao’s Laboratory of Stem Cell Biology, Siegel’s Autoimmune Diseases Research Laboratory and Dr. Raphaela Goldbach-Mansky’s translational autoinflammatory disease section. They learned about new technologies that are helping researchers better understand diseases. Committee members ended their day with a tour of the Clinical Center.

“We greatly value the role that the NIAMS Coalition plays as a partner in outreach and education efforts for arthritis and musculoskeletal and skin diseases,” said Carter.



## WINDOW ART

CONTINUED FROM PAGE 1

### Above, l:

*Annette Weller, a self-taught artist, shows a monkey tree she painted on a Clinical Center window.*

### Above, r:

*A coral tree memorializes Weller's daughter Lauren, who spent 8 years on NIH protocols before succumbing to Ewing's sarcoma in 2011.*

PHOTOS: BELLE WARING, ANNETTE WELLER

She pauses, paint marker in hand, and asks: "Can you put in there how wonderful everybody is?"

Lauren lived with cancer for 8 years. What's astonishing is how much she accomplished and how deeply she touched those around her. She donated her hair to Locks of Love, which provides wigs for cancer patients, and volunteered as a counselor with Camp Fantastic, a summer camp for kids with cancer. She was an active participant with Special Love, a group dedicated to helping young people suffering from pediatric cancers. After completing her master's degree at Frostburg State University, she taught science at Mother Catherine Spalding School in Mechanicsville, Md., and coached volleyball at St. Mary's Ryken High School in Leonardtown, Md. And she married her college sweetheart, who stuck with her through all her treatments.

Before Lauren passed away, she asked her mother to start a fundraiser to bring the families of pediatric patients to the CC.

"NIH brings the child and one caregiver," says Weller. "We want to bring 'em all." So Lauren's legacy now includes "L-Dub's Love," a non-profit group dedicated to assisting and providing resources to families of children receiving cancer treatment.

And Lauren loved music. Along with other patients being treated at the CC, in 2011 she accompanied NIH director Dr. Francis Collins in a special outing to a U2 concert in Baltimore.

"The kids loved her," says Dr. Lori Wiener, NCI's director of psychosocial support and research. "Lauren mobilized, energized and inspired so many children with cancer over the years. She would put her own issues to the side... 'Tell me about you, and how are you today,' is how she

started every conversation. She touched so many people along the way with her smile, energy and warmth... She never gave up hope."

Wiener's role is to support patients and their families during their time at NIH and beyond. Her clinical research includes patient and family mental health, loss and bereavement, staff wellness and interventions—like art—designed to meet the needs of critically ill children and their families.

"There are no adequate words to describe the pain and suffering when a parent has lost a child," she says. Yet art can offer a way to express the indescribable. During Lauren's last inpatient stay, Wiener offered Weller a basket of window paint markers, saying, "Annette, if you are so inclined..."

"I'm not a painter," says Weller, now retired from the postal service, "but I had this tree in my head. So I said what the heck."

She painted a glow-in-the-dark tree on the window of Lauren's room in the CC. With 15 critters in its branches, it was dubbed "the Tree of Life."

"I thought they would wash it off," she says.

Instead, it would become the first of many. The staff did not forget Lauren or her mother's Tree of Life; they had gone through years of changes together, the ups and downs, developmental milestones, birthdays and graduations. After Lauren died, one of the 1NW nurses started a bereavement task force, looking for ways to make the unit more comforting, homelike and interactive for families. She remembered how the kids loved the tree—it made them and their families feel less isolated.

There was real comfort in the image, and Wiener, once a semi-professional photographer, had an eye for that connection. So she contacted Weller





*Weller and her daughter Lauren, who inspired many children with cancer during her years of treatment.*

and asked if she might be willing to return to NIH as a special volunteer.

“We talked about trees symbolized by [their] branches,” says Wiener, “all the different directions [they] can grow, all that trees can carry.”

With a good friend for support, Weller returned to the CC and, on the window of the room next-door to the one where her daughter died, she drew the outline of a new tree. So she didn’t have to feel alone, her friend and Wiener helped by filling it in.

As the project grew, the trees captured the kids’ attention. When a young boy was transferred from “the room with the owl tree” to “the room with the monkey tree,” he wanted the staff to put the owl tree in his new room, says Weller. “So I met with him and placed an owl in the monkey tree. Got a big smile out of him.”

She also met with another child who was preparing for a transplant. “He requested penguins...that was how the penguin tree came about,” she recalls. “I painted it the day before his transplant. He was very sick that day, but was really happy about the window.”

And now, as natural light filters into the rooms, it gives these windows the uplifting beauty of stained glass. This is fitting, because Lauren’s faith was essential to her, says Wiener. “She believed that there would be a tomorrow where she would be joined with those she loved.” Through an advance care planning guide that Lauren helped create, she worked hard to prepare those she loved for life after she was gone. The guide, based on the findings of an NCI clinical protocol, is now available worldwide.

“And she understood why today could be beautiful,” Wiener says.

“Lauren participated in many NIH studies,” she continues. “She helped advance science and perhaps even more importantly, she advanced a dignified way to live with cancer.”

Her mother continues Lauren’s legacy of hope and service. “It’s really cathartic,” she said. “It helps me say goodbye a little bit more every time I do one.”



*Members of the UNITE consortium—representing the United Kingdom, China and the United States—are working to improve our understanding of immune-related eye disease.*

## NEI Expands International Research Consortium

Representatives of the National Eye Institute took part in a signing ceremony recently with leaders from research institutions in China and England to expand a collaborative international research program. Called UNITE, short for Universities and National Institutes Transatlantic Eye Consortium for Human Ocular Immunology, the consortium helps advance international collaboration in the study of immune-related eye disease. The signing ceremony and discussions took place at the Association for Research in Vision and Ophthalmology meeting in Seattle.

The consortium builds upon an earlier agreement that was signed in 2012 between NEI and the National Institute for Health Research, the part of the United Kingdom government that funds and conducts biomedical research. British participants include Moorfields Eye Hospital and University College London Institute of Ophthalmology, University Hospitals Bristol and the University of Bristol. The latest agreement now adds two leading institutions from China to the consortium—Zhongshan Ophthalmic Center in Guangzhou and Chinese University of Hong Kong.

Participating members hope to increase our understanding of immune system mechanisms that lead to ocular inflammation in such diseases as uveitis, age-related macular degeneration (AMD) and diabetic retinopathy. Their goal is to translate observations from laboratory studies into new human trials. Among other activities, NEI and U.K. researchers have already conducted scientific exchanges, pursued joint intellectual property rights for targeted drug therapies and collaborated on several clinical trials on uveitis, AMD and diabetic macular edema. To help aid face-to-face communication, the researchers meet weekly by Skype and are planning a UNITE symposium for the end of 2013.

UNITE members share technologies and biological material from their patient populations and experimental models. They also share protocols to help standardize clinical practice in the area of human ocular immunology.

“The relationships we are fostering transcend what we normally think of as scientific collaboration,” said Dr. Gyan “John” Prakash, associate director for international programs at NEI. “These scientists are sharing data, materials, protocols and personnel with each other in the hope of addressing some of the most debilitating eye diseases worldwide. It’s almost as if the researchers are working in the same laboratory—only one that spans three continents.”

“Disease knows no boundaries,” agreed Dr. Robert Nussenblatt, chief of NEI’s Laboratory of Immunology and a lead scientist in the project. “Extending UNITE to include China can only help in understanding disease on an international scale. Greater understanding can speed healing.”

## GALEA

CONTINUED FROM PAGE 1



*Galea (c) speaks with OBSSR acting deputy director Dr. Patricia Mabry and Dr. G. Stephane Philogene, OBSSR associate director for policy and planning.*

PHOTOS: ERNIE BRANSON

But reality exists in context. And to ignore context, argues Dr. Sandro Galea, physician and Gelman professor of epidemiology at Columbia's Mailman School of Public Health, is a cog-

nitive mistake with real consequences for both biomedical science and public health. He recently visited NIH to argue for a re-engagement in the behavioral/social sciences in "Is It All About Me? The Role of Public Health in an Era of Personalized Medicine." His lecture was sponsored by the Office of Behavioral and Social Sciences Research.

Galea began with a question from Mario Balotelli, the international soccer star, flaunting a T-shirt stamped "Why Always Me?"

Surely, Balotelli is a great striker, but he also plays for a great team with guys who pass him the ball so he can score. His boast is a "fundamental attribution error"—the tendency to overestimate the effect of the individual and to ignore context.

This shows Galea's central premise: We in biomedicine are undervaluing context. Despite the promise of personalized medicine, our focus on the individually curative is crowding out our responsibility for disease and disability prevention across populations.

"I realize that coming to NIH to talk about public health is a little bit incongruous, but that's part of my intention," said Galea, who has a wry sense of humor. "I mean to issue a bit of a provocation to see what you all think about it. In an era when we're thinking about a narrower approach, that approach is excluding approaches that we not only *should* take, but we *must* take if we're going to get our science right," he said.

He offered a caveat: "Nothing in my talk is taking on genomics. I come not to bury genomics but to elevate public health," he said.

In Galea's own primary research focus, he has documented the mental health consequences of mass trauma and conflicts, including the 9/11

attacks, Hurricane Katrina, conflicts in sub-Saharan Africa and the American wars in Iraq and Afghanistan.

Our central motivation should be improving the health of all, he insisted. Yet our enthusiasm for the individual, particularly for genomics, has become "a riveting distraction" from focusing on other fundamental drivers of health.

"Here is the perhaps inevitable syllogism," he said. "Here is where we make our mistake."

A syllogism goes like this: A = B. And B = C. Therefore, A = C.

So: Penguins are black and white. Some old movies are black and white. Therefore, some penguins are old movies.

You can see the problem.

Galea says we've applied this flawed logic to our investment in personalized medicine. We know that genetic mutations cause disease (A = B). We know that we can genotype individuals (B = C). Therefore, we think we can predict disease or treatment response in individuals (A = C).

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***Galea's central premise: We in biomedicine are undervaluing context. Despite the promise of personalized medicine, our focus on the individually curative is crowding out our responsibility for disease and disability prevention across populations.***

This idea is compelling, he says, but it is based on a fallacy. It is mathematically impossible to predict who is going to develop disease by looking only at genetic factors.

For example, a mega-analysis of genome-wide association studies for major depressive disorder found no "robust and replicable findings."

Meanwhile, an analysis of life expectancy at birth for U.S. white males shows a 15-year gap according to county, 1997-2001. The gap was "not driven by heterogeneity in genes or behavior. It was something greater than that." Where we live affects our health so much that "to put all our eggs in the individualist basket may not be the smartest thing after all."

Galea offered several other published studies and mathematical simulation models showing





*Galea said he meant to be somewhat provocative in urging NIH to rethink research emphases.*

that disease can be understood only if genetic and social/environmental risk factors are modeled simultaneously over time.

"The dominant research in the biomedical establishment keeps asking why one individual in the population has a systolic blood pressure of 140, rather than asking the larger question," he said. "Why is it that London civil servants' curve [of data showing relatively higher blood pressure values] is there, while Kenyan nomads' curve [with lower, healthier values] is over here? Were we able to understand that, we might be able to move the whole curve."

This applies to other risk factors as well. "There is an association between cholesterol and heart disease, but the problem is that association is true at the population level. At the individual level it tells you next to nothing as to whether I, with a serum cholesterol of 270, will develop heart disease."

The genetic revolution has brought important triumphs such as pharmacogenomics, diagnostics for breast cancer and neonatal screening.

Yet "we keep investing more and more money in better mousetraps, in better sequencing approaches...Of course these methods are valid, but no matter how good you get at identifying individual characteristics, you are not going to be able to predict individual health."

In a discussion after the talk, Galea was asked about the importance of disease mechanisms.

"A subset of population health is curative medicine," he said. "I think the mechanistic knowledge is very important for the practice of curative medicine, and, from the point of view of science, of understanding nature. My worry is about that at the expense of all else."

The videocast is archived at <http://videocast.nih.gov/summary.asp?live=12723>. 📺

## Integrating Palliative, Oncology Care Shows Benefit

When palliative care is introduced early in the course of advanced cancer, it has been shown to enhance quality of life and improve mood. Dr. Jennifer Temel, an NINR grantee, is one of the leading researchers in this field and gained national attention when she and her colleagues published a paper in the *New England Journal of Medicine* titled, "Early palliative care for patients with metastatic non-small-cell lung cancer." The study showed the benefits of early introduction of palliative care "on patient-reported outcomes and end-of-life care among ambulatory patients with newly diagnosed disease." The study, along with her more recent work, laid the foundation for the presentation Temel gave to the NIH end-of-life and palliative care special interest group and guests recently.

The lecture was hosted by NINR. Research into end-of-life and palliative care is a focus for the institute, as reflected in its strategic plan. NINR director Dr. Patricia Grady welcomed Temel and emphasized the importance of the scientific advances being made in this field. In an NIH radio interview last fall, Grady said, "When palliative care is available, the symptoms of pain or distress are usually reduced so that patients are able to enjoy better quality of life."

In addition to improvements in mood and quality of life, integrating palliative care early in the course of a cancer illness has been shown to affect chemotherapy use. During the lecture, Temel discussed a study that found that patients who received palliative care services had optimal timing of their final chemotherapy administration and transition to hospice; both factors are measures of quality of end-of-life care. She noted that it is new cancer treatments along with palliative care to manage pain and other symptoms that have enabled patients to live more fully, more comfortably, more optimally and with a sense of control of their advanced care management.

Temel, clinical director of thoracic oncology at Massachusetts General Hospital and associate director of the Dana-Farber/Partners Cancer Care hematology/oncology fellowship, also presented data from a study she is currently conducting, which is funded by NINR. The study will compare early integrated palliative and oncology care versus oncology care alone in 350 patients with advanced thoracic and gastrointestinal malignancies. To close the lecture, Temel shared ideas and plans for future directions in her research.

## Volunteers Needed with Chronic Liver Disease

NIDDK seeks volunteers 18 and older with chronic liver disease such as hepatitis, fatty liver and cirrhosis to join a research study. Fatigue is common in people with liver disease and can severely affect quality of life. Researchers want to learn what causes fatigue in people with liver disease. You do not need to have fatigue to participate in this study. You will complete a sleep diary for 1 week, answer questionnaires and have blood draws. You will spend 1 night at the Clinical Center where your sleep will be monitored (sleep study). Study-related procedures are provided at no cost. Compensation may be provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 13-DK-0142.



*NINR director Dr. Patricia Grady (l) and Dr. Jennifer Temel at the end-of-life and palliative care special interest group lecture*



*Drs. Dmitry Gordenin (l) and Steven Roberts of NIEHS and their colleagues found that naturally produced mutations are just as powerful as known cancer-causing agents in producing tumors.*

PHOTO: NIEHS

### Proteins Involved in Immunity Potentially Cause Cancer, NIH Scientists Say

A set of proteins involved in the body's natural defenses produces a large number of mutations in human DNA, according to a study led by researchers at NIH. The findings suggest that these naturally produced mutations are just as powerful as known cancer-causing agents in producing tumors.

The proteins are part of a group called apolipoprotein B mRNA-editing enzyme catalytic polypeptide-like (APOBEC) cytidine deaminases. The investigators found that APOBEC mutations can outnumber all other mutations in some cancers, accounting for over two-thirds in some bladder, cervical, breast, head and neck and lung tumors.

The scientists published their findings online July 14 in *Nature Genetics*. Dr. Dmitry Gordenin, a senior associate scientist at NIEHS, said scientists knew the main functions of APOBEC cytidine deaminases were to inactivate viruses that attack the body and prevent ancient viruses present in the human genome from moving around and causing disrupting mutations. Because they are so important to normal physiology, he and his collaborators were surprised to find a dark side to them—that of mutating human chromosomal DNA.

“The presence of APOBEC clusters in the genome of tumor cells indicates that APOBEC enzymes could also have caused many mutations across the genome,” Gordenin said.

Gordenin's team at NIEHS and collaborators at medical centers looked for signs of genome-wide APOBEC mutagenesis in cancers listed in The Cancer Genome Atlas. Using APOBEC's distinctive DNA mutational signature, they examined approximately 1 million mutations in 2,680 cancer samples and found that, in some tumors, nearly 70 percent of mutations in a given specimen resulted from APOBEC mutagenesis. The mutation pattern, which appeared in clusters and individual mutations, could affect many cancer-associated genes.

Dr. Steven Roberts, a postdoctoral fellow who works with Gordenin, explained that since APOBECs are regulated by the immune system, which is responsive to many environmental factors, he believes there may be a significant environmental component to APOBEC mutagenesis. “We hope

that determining the environmental link to these mutations will lead to viable cancer prevention strategies,” he said.

### NIH Study Identifies Brain Circuits Involved in Learning, Decision-Making

Research from NIH has identified neural circuits in mice that are involved in the ability to learn and alter behaviors. The findings help explain the brain processes that govern choice and the ability to adapt behavior based on the end results.

Researchers think this might provide insight into patterns of compulsive behavior such as alcoholism and other addictions.

“Much remains to be understood about exactly how the brain strikes the balance between learning a behavioral response that is consistently rewarded, versus retaining the flexibility to switch to a new, better response,” said Dr. Kenneth Warren, acting NIAAA director. “These findings give new insight into the process and how it can go awry.”

The study, published online in *Nature Neuroscience*, indicates that specific circuits in the forebrain play a critical role in choice and adaptive learning.

### NIH Scientists Assess History, Pandemic Potential of H7 Influenza Viruses

The emergence of a novel H7N9 avian influenza virus in humans in China has raised questions about its pandemic potential as well as that of related influenza viruses. In a commentary published online July 9 in *mBio*, scientists at NIAID address these questions by evaluating past outbreaks of H7 subtype influenza viruses among mammals and birds and comparing H7 viruses with other avian influenza viruses and strains.

In recent decades, the scientists write, avian H7 viruses have caused numerous influenza outbreaks among poultry in Europe and North America. Since at least 1918, none of these poultry-adapted viruses has evolved to widely infect humans or cause a pandemic. However, some of them have stably adapted to infect mammals such as horses, suggesting that these viruses might become adapted to and transmissible among other mammals, including humans. In particular, the novel H7N9 virus shares some genes with the H9N2 influenza virus subtype, which has also infected humans. This genetic relatedness may predispose it to more easily adapt to humans than other H7 viruses.

The possibility that H7N9 or another H7 virus may adapt to easily infect humans highlights a need for more research on how avian influenza strains adapt to mammals, especially humans, and better integration of flu research between human and veterinary public health specialists, study authors conclude.





## Second Annual Pheo Symposium Draws International Crowd

By Rebecca Lazeration

Scientists, students and patients from around the world gathered recently at NIH for the second annual International Patient Symposium on Pheochromocytoma. The event, sponsored by the Pheo Para Alliance, focused on current studies and the future of pheochromocytoma and paraganglioma research. Pheochromocytomas are tumors that originate inside the adrenal glands and paragangliomas are similar tumors that form outside the adrenals.

The symposium, held on campus at Bldg. 60, also included presentations on treatments for these conditions.

"It is important to have this conference because it brings together patients and researchers. It is important to be brought together because people next door and around the world will benefit," said NICHD director Dr. Alan Guttmacher as he opened the symposium.

"There are no national or international groups that study pheochromocytoma and that is the most important thing to fix," said Dr. Karel Pacak, a senior investigator in NICHD's section on medical neuroendocrinology and long-time pheochromocytoma researcher. "It is important that we begin working with others to advance the research on these rare tumors. Together we stand a chance, separately we fail."

Pacak spoke twice on the opening day of the conference, outlining the most recent research into the genes that are linked with the onset of pheochromocytoma and paraganglioma and describing upcoming research into positron emission tomography scans and other imaging techniques for pheochromocytoma and paraganglioma at NIH. He explained how 50 percent of pheochromocytoma and paraganglioma cases are not diagnosed or are misdiagnosed and are only found during autopsy. He also said that with "a lack of interest from



*Above, from l:*

*NICHD researcher Dr. Karel Pacak (l) and NICHD director Dr. Alan Guttmacher kicked off the symposium.*

*Spelling out Team Pacak are (from l) Victoria Martucci, Clarissa Samson, Eric Laplano, Ivy Nisce and Alekhya Reddy, volunteers in NICHD's Program in Reproductive and Adult Endocrinology.*

*At right, NIH director Dr. Francis Collins sang and played his guitar as part of a trio.*

PHOTOS: BILL BRANSON



young clinicians," the outlook for pheochromocytoma and paraganglioma research was not positive.

At the end of the first day of the conference, a musical performance took place, featuring Laura Pole and Greg Trafidlo, two members of the group Trifolkal. The two sang upbeat songs based on Pole's knowledge of treatment from her time as a hospice nurse. NIH director Dr. Francis Collins joined the two to complete the trio.

Pole said the performance was meant to "spread the positive message of healing" through songs such as "Sanctuary" and "If Not Now, Tell Me When."

"What is the difference between wellness and illness?" she asked: "We and I." She explained that "wellness, brought through healing, is something that should never be done alone. Family and friends are what make the difference."

She continued, "Healing is different than curing. Curing is getting rid of an illness. Healing is what brings us back to a sense of wholeness."

Wayne Zandbergen, who hosted the symposium, is the founding member of the Pheo Para Alliance, a support group that provides resources to patients and physicians dealing with pheochromocytoma and paraganglioma.

"This is not a symposium for the M.D.s and Ph.D.s," he said. "We are here for the guy with a practice in Iowa. We are here to tell him what it will mean for him and his patient that the patient has pheochromocytoma. Those are the people who really matter." 🎸





At left, the Tree of Hippocrates, planted in 1961, is bare and leafless despite a lush, wet summer. Above, a plaque in front of the tree explains its significance.

## Harm Comes to 'Tree of Hippocrates'

By Sarah Krosnick

Planted in 1961 as a gift from the Greek government, the Tree of Hippocrates (*Plantanus orientalis*) has graced the lawn across Center Dr. from the National Library of Medicine as a symbol of the Hippocratic Oath and Hippocrates' medical innovations. The tree's health has declined in its more than half-century reign, resulting in a failure to re-leaf during the spring of this year.

Legend states that Hippocrates taught medical students under the original tree, located in Cos (or Kos), Greece, thousands of years ago. Subsequent cuttings of the tree have allowed for offspring trees to be placed around the world at the Greek government's discretion. Lynn Mueller, NIH landscape architect, estimates that "we may have the only...Hippocrates tree." While other medical institutions in the United States have seedling trees from the Tree of Hippocrates, NIH has a direct cutting of the tree.

NIH was initially presented with two trees to commemorate NLM's new building (Bldg. 38), although only one survived, creating a dilemma once the surviving tree began to deteriorate in 1990. The Grounds Maintenance and Landscaping Branch began a decade-long attempt to restore the tree. Despite a program that included deep-root feedings and fungicide injections, the tree showed no signs of regaining strength. In addition to long-term distress, the tree fell victim to a severe anthracnose fungal outbreak this spring, further expediting its decline.

Since the early 1990s, Mueller has attempted to find a replacement for the tree that also features a direct ancestry with the original tree in order to preserve the plant's rich history. Initially, he worked to clone NIH's tree himself, but the cloning process instead resulted in hybrid offspring. After contacting other medical institutions with Tree of Hippocrates seedlings and even the Greek embassy, Mueller was still unable to find a pure version of the tree.

In the late 1990s, Mueller outsourced his cloning attempts to professional nurseries on the east coast, without success. In 2003, he discovered the Champion Tree Project in Copemish, Mich., which he describes as "a group who began trying to clone the remaining giant or champion trees around the U.S. and eventually the world." Although the Tree of Hippocrates was not the focus of the project's preservation efforts, the group decided to attempt to clone the Tree of Hippocrates' cuttings.

Additionally, Dr. Walter J. Pories, professor of surgery, biochemistry and exercise sports science at East Carolina University, took an interest in Mueller's project and began to nurse seedlings at his university. According to Mueller, two seedlings from Pories' efforts were planted at NIH in 2009 and "are flourishing and growing at Bldg. 22 and in a reforestation area near parking lot 41B."

This past spring's unusually cool, damp weather ultimately sapped the 1961 tree's remaining energy and caused the tree to fail to re-leaf. Luckily, the Champion Tree Project was successful in cloning the cuttings from 2003 and has produced two viable options for NIH to plant in the fall if the current tree does not re-leaf by the end of summer.

One tree will replace the current Tree of Hippocrates while the other will be planted elsewhere on campus as a backup should the first option not survive. Dr. Richard Wyatt of the Office of Intramural Research hopes that the original tree can be repurposed if it is cut down. "I am sure we can use the trunk to craft awards!" he said.

After nearly two decades of attempting to clone the historically significant tree, Mueller said he "hope[s] that this new tree will flourish for the next 100 years and represent the oath and teaching of Hippocrates here on the NIH campus." 🌱